UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/571,291	11/28/2006	Pascale Gaillard	GAILLARD2	6383

1444 7590 07/30/2010

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
07/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/571,291	GAILLARD ET AL.	
	Examiner	Art Unit	
	/Venkataraman Balasubramanian/	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response filed on 07/15/2009 requesting entry of amended claims filed on 06/16/2010, is made of record. Claims 1-8 and 10-14 are now pending. Upon further consideration the Finality of the previous office action is withdrawn to make the following new grounds of rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Halazy et al., WO 01/47920 in view of Bennett et al., Current Opinion in Pharmacology 2003, 3:420–425(or Kaneto-I, Kaneto-II, Kaneto-III or Hotamisligil) and Gatlin et al., US 6,559,188 .

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Halazy et al., teaches several benzazole compounds useful for treating disorder of immune system cancer, which include instant compounds. See page 9, formula I and

note definition of the X, G, L, R^1, and R^2. Note when X is S, G= pyrimidinyl with L substituents, with given definition of other variable choices, the compounds taught by Halazy et al., include instant compounds. See pages 9-24 for details of the preferred embodiments, species and process of making these compounds. See entire document. Particularly, see pages 28-54, for examples of compounds made. Although Halazy et al. teaches several benzothiazole compounds, Halazy et al., does not exemplify all the compounds of genus of compound of formula I shown in page 9, wherein X=S. But Halazy et al., teaches equivalency of alternate choices of all variables including X, with the compounds taught in pages 9-55 with those generically claimed in page 9.

Currently amended claims 1-8 and 10-14 related to method of use different from those taught by Halazy et al. However, Halazy et al., teaches such benzothiazoles are useful in inhibiting JNKs and JNKs are known at the time of instant invention to be implicated in metabolic disorder mediated by insulin resistance or hyperglycemia such as diabetes type II, inadequate glucose tolerance and obesity.

For example, Bennett et al., teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity.

Similarly, the all the secondary references Kaneto-I, Kaneto-II, Kaneto-III and Hotamisligil teach usefulness of JNK inhibitors for treating Type-II diabetes. See entire document.

In addition, currently presented method of use claims recite additional active ingredients for a combination therapy.

Again, it is known at the time of instant invention the effectiveness of treatment of

diabetes can be increased by using a combination of antidiabetic agents.

For example, Gatlin teaches use combination of various anti-diabetic agents including PPAR gamma agonists claimed in the currently amended claims. See entire document. Especially, see column1-5, 11-14 and 21-22 for combination of active ingredients for treating diabetes.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made based on to combined the teaching of Halazy and Bennett and Gatlin to make various compounds of formula I as permitted by the reference using teachings of Halazy, and expect resulting compounds to possess the uses taught by the combined art use them in combination therapy in view of the teaching outline above.

This rejection is similar to that made in the previous office action but now limited to currently pending claims and includes additional supporting prior art. Applicants' traversal to overcome this rejection is not persuasive. First of all, the compounds taught by Halazy are same as that of instant claims. Instant specification on page 2 clearly acknowledges this. The compounds of Halazy are JNK inhibitors. Thus, administering the genus of compounds of Halazy (that is instant genus of compounds) would inhibit JNK. Whatever negative attributes applicants offer for method of use of compounds of Halazy would be equally applicable to instant compounds.

Bennett et al., clearly teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity as seen pages 420-422. Instant claims recite the same. Applicants argued, pointing page that while instant compounds decreases insulin

and glucose, Bennett teaches lowering of plasma glucose but not plasma insulin. This is not correct. Contrary to applicants' urging, the Figure 2 shown in page 422 of Bennett clearly shows lowering of plasma glucose and insulin. And it is also improper comparison as applicants have measured plasma glucose level and plasma insulin level after 4 hr as pointed by applicants(see page 29, lines 18-21).

Thrust of applicants' argument is that Bennett's compound increase insulin level, based on the data 20 ng to 30 ng during first 15 minutes of administration, while instant compounds decrease insulin level. However, as seen in Figure 2, Bennett teaches decrease in insulin level at 120 minutes. Applicants have not shown that instant compound does not raise initial insulin level before decreasing. Applicants' measurement of insulin level appears to be at 4hrs after administration of the instant compound.

Contrary to applicants' urging pointing column 1 of page 422, Bennett in this column clearly teaches usefulness of JNK inhibitors in treating insulin resistance, diabees and obesity as reproduced below:

"We have studied the performance of a small molecule JNK inhibitor (Celgene Corporation; CC105) in the leptin-receptor-deficient model of diabetes and obesity, the db/db mouse. This strain exhibits an early-phase hyper- insulinemia followed by progressive pancreatic failure and hypoinsulinemia from about six weeks of age. This leads to increased blood glucose and obesity. After 17 days of oral dosing with the JNK inhibitor, we observed significantly lower blood glucose and higher insulin levels (Figure 2). After oral glucose loading, we observed increased plasma insulin and improved

glucose control in animals treated with the JNK inhibitor (Figure 2). Ex vivo analysis of pancreatic islet cells showed marked improvements in acinar recovery and morphology, as well as insulin release following high glucose stimulation (Figure 3). This preliminary pharmacological data shows striking parallels to the observations made using Jnk1-I-ob/ob mice. Further studies in appropriate models should define the potential of JNK inhibitors in treating insulin resistance and obesity".

Clearly, based on the significant lowering of blood sugar, one would expect JNK inhibitors to be useful for treating Type-II diabetes and obesity. The entire document, and especially the concluding paragraph clearly lends support for JNK inhibitors to treat diabetes, insulin resistance and obesity. It is held that, although there is no reason to doubt the compounds of Halazy were not useful for treating insulin resistance, even if they were not useful for treating insulin resistance, the compounds of Halazy would be useful for treating diabetes and obesity.

It should also be noted that applicants' argument that instant compounds lower insulin and hence useful for treating metabolic disorders claimed therein is also not persuasive for another reason. Method of use claims 9 and 10 clearly recites use of additional insulin selected from group consisting of a rapid acting insulin, an intermediate acting insulin, a long acting insulin, a combination of intermediate and rapid acting insulins. Thus, applicants first argues that Bennett's compounds raise insulin levels while instant compounds do not and then for the actual method of use applicants states additional insulin is needed to be effectively treat claimed metabolic disorders. This is clearly contradictory to applicants' criticisms of Bennett. Hence, it

appears that the decreasing insulin level appears to be not critical.

For reasons stated above this rejection is proper and is maintained.

Claims 1-8 and 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard et al., WO 03/091249 in view of Bennett et al., Current Opinion in Pharmacology 2003, 3:420–425 or Kaneto-I, Kaneto-II, Kaneto-III or Hotamisligil) and Gatlin et al., US 6,559,188. or Fine 6,376,549.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Gaillard et al., teaches several benzothiazole compounds useful for treating ischemic disorders, which include instant compounds. See page 3, formula A and note

definition of the X, G, R^1, and R^2. Note when X is S, G= pyrimidinyl with substituents, with given definition of other variable choices, the compounds taught by Gaillard et al., include instant compounds. See pages 3-17 for details of the preferred embodiments, species and process of making these compounds. See entire document. Particularly, see pages 20-29, for examples of compounds made.

Although Gaillard et al. teaches several benzothiazole compounds, Gaillard et al., does not exemplify all the compounds of genus of compound of formula A shown in page 3, wherein X=S. But Gaillard et al., teaches equivalency of alternate choices of all variables with the compounds taught in pages 20-29 with those generically claimed in page 3. Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make various compounds of formula A as permitted by the reference using teachings of Gaillard et al., and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Currently amended claims 1-10,13 and 15-20 related to method of use different from those taught by Gaillard et al. However, Gaillard et al., teaches such benzothiazoles are useful in inhibiting JNKs and JNKs are known at the time of instant invention to be implicated in metabolic disorder mediated by insulin resistance or hyperglycemia such as diabetes type II, inadequate glucose tolerance and obesity.

For example, Bennett et al., teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity.

Similarly, the all the secondary references Kaneto-I, Kaneto-II, Kaneto-III and Hotamisligil teach usefulness of JNK inhibitors for treating Type-II diabetes. See entire

document.

In addition, currently presented method of use claims recite additional active ingredients for a combination therapy.

Again, it is known at the time of instant invention the effectiveness of treatment of diabetes can be increased by using a combination of antidiabetic agents.

For example, Gatlin teaches use combination of various anti-diabetic agents including PPAR gamma agonists claimed in the currently amended claims. See entire document. Especially, see column1-5, 11-14 and 21-22 for combination of active ingredients for treating diabetes.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention was made based on to combined the teaching of Gaillard and Bennett to make various compounds of formula I as permitted by the reference using teachings of Gaillard, and expect resulting compounds to possess the uses taught by the combined art in combination therapy in view of the equivalency teaching outline above.

This rejection is same as made in the previous office action. Applicants' traversal to overcome this rejection is not persuasive. First of all, the compounds taught by Halazy are same as that of instant claims and they are JNK inhibitors. Instant specification on page 2 clearly acknowledges this. The compounds of Gaillard are JNK inhibitors. Thus, administering the genus of compounds Gaillard that is instant genus of compounds would inhibit JNK. Whatever negative attributes applicants offer for method of use of compounds of Gaillard would be equally applicable to instant compounds.

Bennett et al., clearly teaches JNK inhibitors to be useful in treating insulin resistance, diabetes and obesity as seen pages 420-422. Instant claims recite the same. Applicants argued, pointing page that while instant compounds decreases insulin and glucose, Bennett did teaches lowering of plasma glucose but not plasma insulin. This is not correct. Contrary to applicants' urging, the Figure 2 shown in page 422 of Bennett clearly shows lowering of plasma glucose and insulin. And it is also improper comparison as applicants have measured plasma glucose level and plasma insulin level after 4 hr as pointed by applicants(see page 29, lines 18-21).

Thrust of applicants' argument is that Bennett's compound increase insulin level, based on the data 20 ng to 30 ng during first 15 minutes of administration, while instant compounds decrease insulin level. However, as seen in Figure 2, Bennett teaches decrease in insulin level at 120 minutes. Applicants have not shown that instant compound does not raise initial insulin level before decreasing. Applicants' measurement of insulin level appears to be at 4hrs after administration of the instant compound. Contrary to applicants' urging pointing column 1 of page 422, Bennett in this column clearly teaches usefulness of JNK inhibitors in treating insulin resistance and obesity as reproduced below:

"We have studied the performance of a small molecule JNK inhibitor (Celgene Corporation; CC105) in the leptin-receptor-deficient model of diabetes and obesity, the db/db mouse. This strain exhibits an early-phase hyper- insulinemia followed by progressive pancreatic failure and hypoinsulinemia from about six weeks of age. This leads to increased blood glucose and obesity. After 17 days of oral dosing with the JNK

inhibitor, we observed significantly lower blood glucose and higher insulin levels (Figure 2). After oral glucose loading, we observed increased plasma insulin and improved glucose control in animals treated with the JNK inhibitor (Figure 2). Ex vivo analysis of pancreatic islet cells showed marked improvements in acinar recovery and morphology, as well as insulin release following high glucose stimulation (Figure 3). This preliminary pharmacological data shows striking parallels to the observations made using Jnk1-I-ob/ob mice. Further studies in appropriate models should define the potential of JNK inhibitors in treating insulin resistance and obesity".

Clearly, based on the significant lowering of blood sugar, one would expect JNK inhibitors to be useful for treating Type-II diabetes and obesity. The entire document, and especially the concluding paragraph clearly lends support for JNK inhibitors to treat diabetes, insulin resistance and obesity. It is held that, although there is no reason to doubt the compounds of Gaillard were not useful for treating insulin resistance, even if they were not useful for treating insulin resistance, the compounds of Gaillard would be useful for treating diabetes and obesity.

It should also be noted that applicants' argument that instant compounds lower insulin and hence useful for treating metabolic disorders claimed therein is also not persuasive for another reason. Method of use claims 9 and 10 clearly recites use of additional insulin selected from group consisting of a rapid acting insulin, an intermediate acting insulin, a long acting insulin, a combination of intermediate and rapid acting insulins. Thus, applicants first argues that Bennett's compounds raise insulin levels while instant compounds do not and then for the actual method of use

applicants states additional insulin is needed to be effectively treat claimed metabolic disorders. This is clearly contradictory to applicants' criticisms of Bennett. Hence, it appears that the decreasing insulin level by instant compounds appears to be not critical. For reasons stated above this rejection is proper and is maintained.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624